Armed Forces College of Medicine

AFCM

Sodium and Glucose Reabsorption

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Define sites of Na reabsorption
2. Describe Na reabsorption by different segments of renal tubulem
3. List manifestations of Bartter syndrome
4. Describe glomerulo – tubular balance

Lecture Plan

1. Part 1 (5 min) Introduction
2. Part 2 (35 min) Main lecture
3. Part 3 (5 min) Summary
4. Lecture Quiz (5 min)

Introduction

Na^+ Handling by the Renal Tubules:

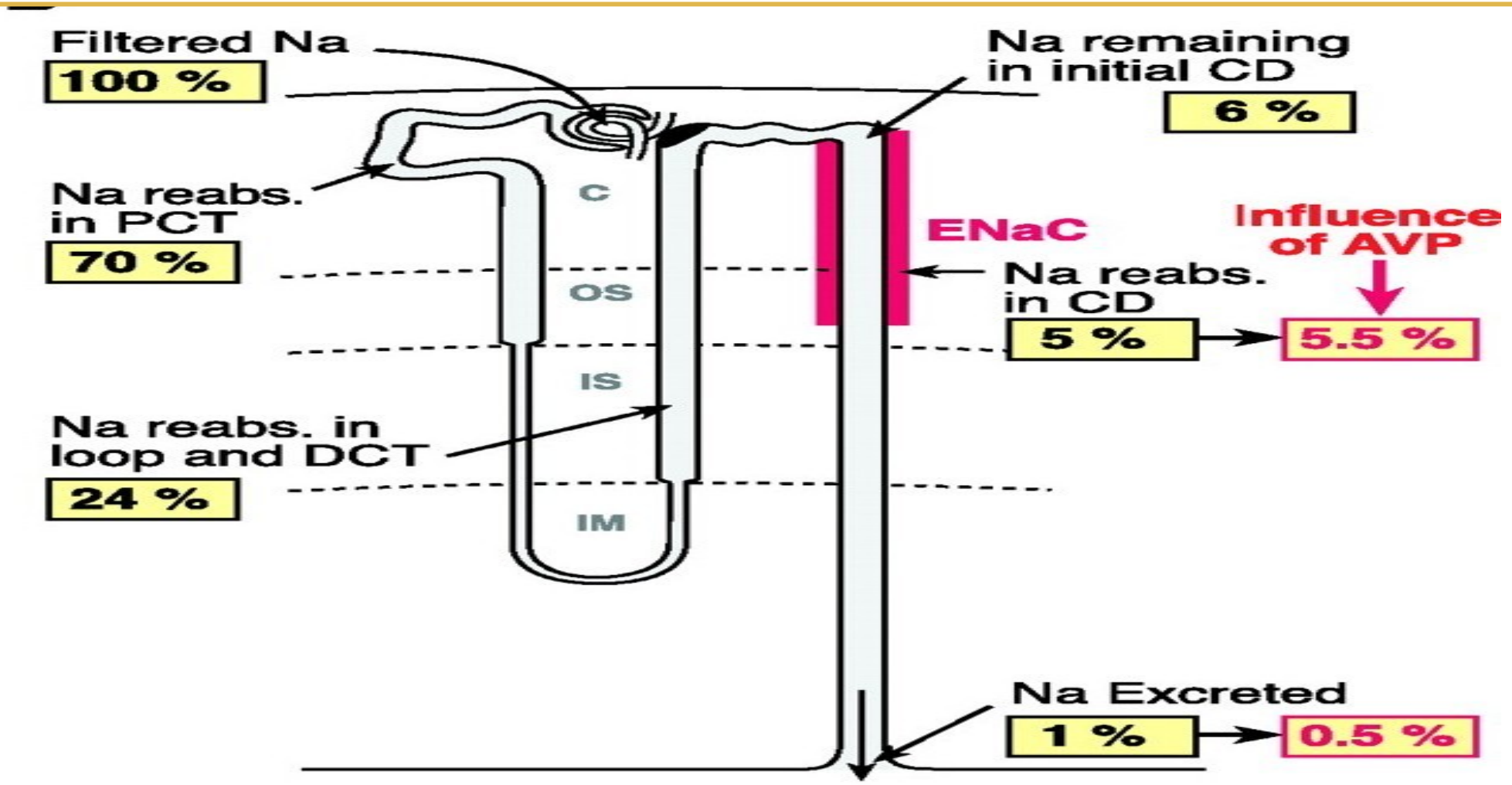
- Na^+ is reabsorbed out of all portions of the renal tubule except the thin descending segment of the loop of Henle.

- 90% of the energy consumed by kidney is used for active transport of Na^+

- The reabsorption of Na+ is coupled with:

- - Reabsorption of glucose “ amino acids and chloride”
- - Reabsorption of H_2O by osmosis
- - Secretion of K^+
- - HCO_3^- reabsorption and H^+ secretion

Na^+ Reabsorption in the Different Segments of the Renal



:Proximal Tubule .1

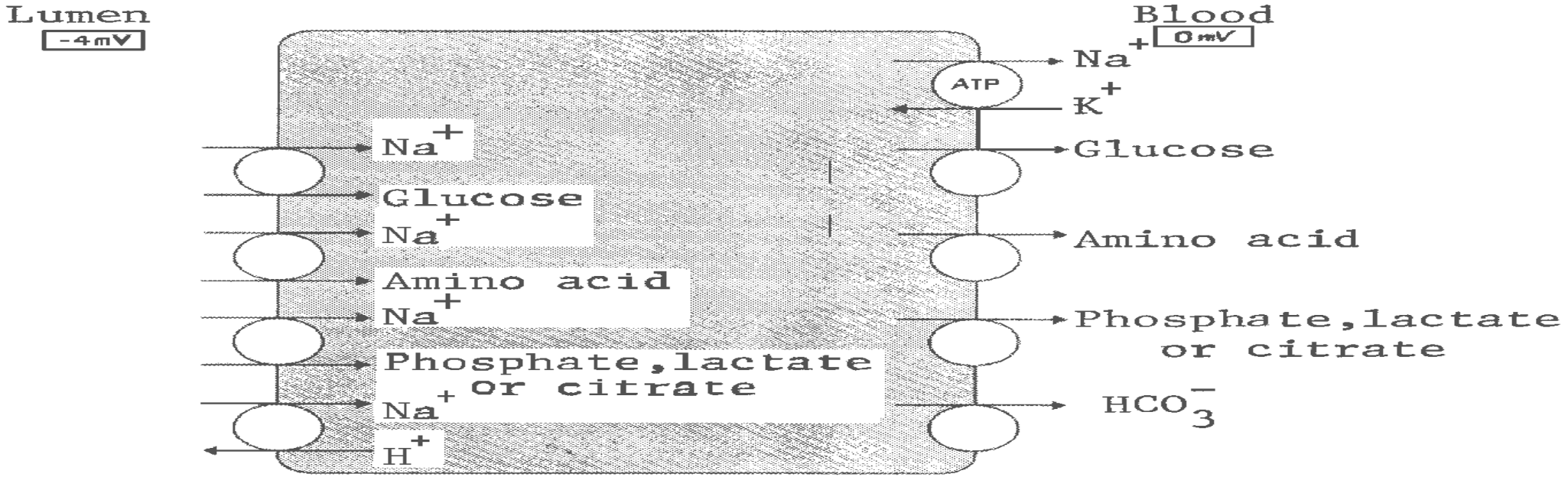
- 65% of the filtered load of Na^+ is reabsorbed by the proximal tubule.

- This reabsorptive process is active and depends on the action of the basolateral membrane Na^+ K^+ -pump, to keep intracellular Na^+ concentration low.

- Na^+ reabsorption by PCT is an active. . Early and late proximal tubules are different as regards the anions and other solutes that accompany Na^+.

:a) First half of The Proximal Tubule

- Na^+ is reabsorbed by co-transport along with glucose, amino acids, sulphate, Pi, organic acids (lactate and citrate).



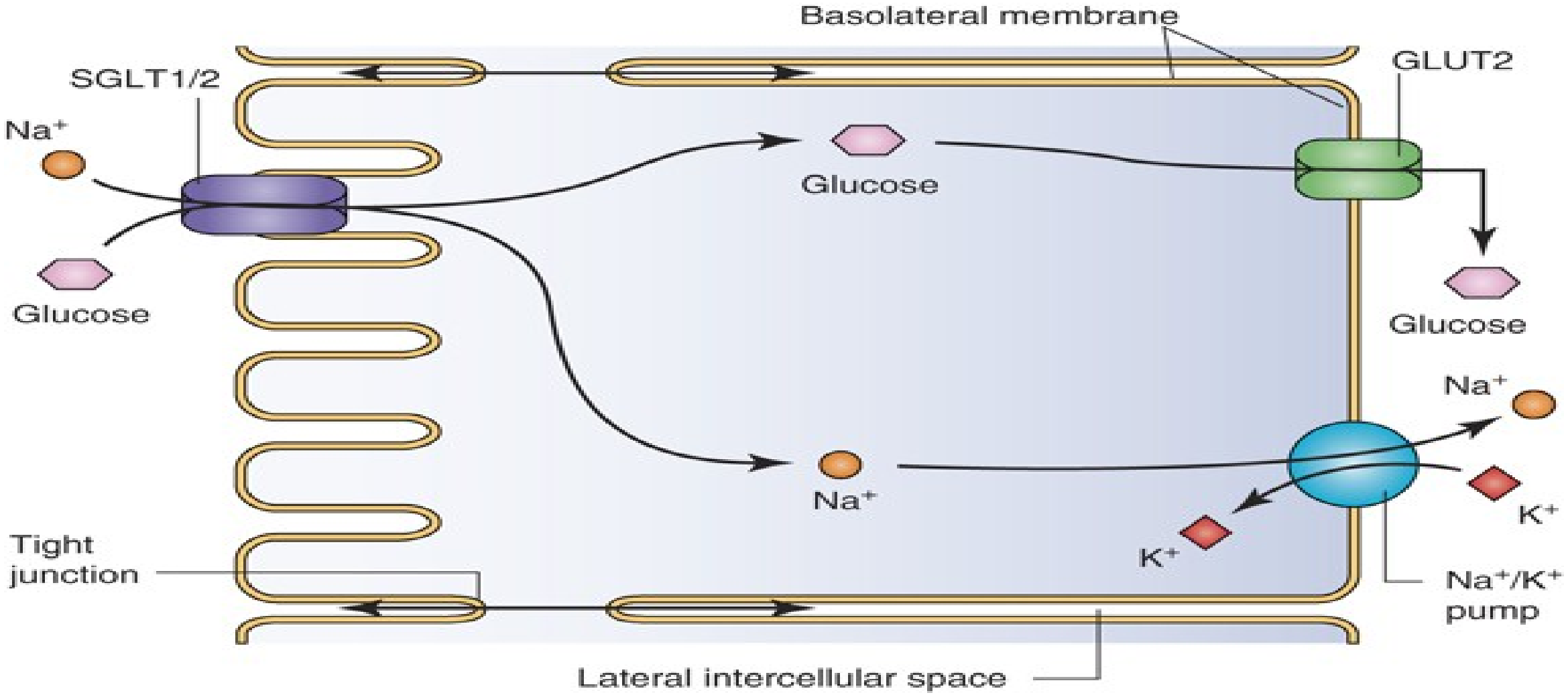
:a) First half of The Proximal Tubule

- Cotransport processes account for the reabsorption of all the filtered glucose and amino acids.

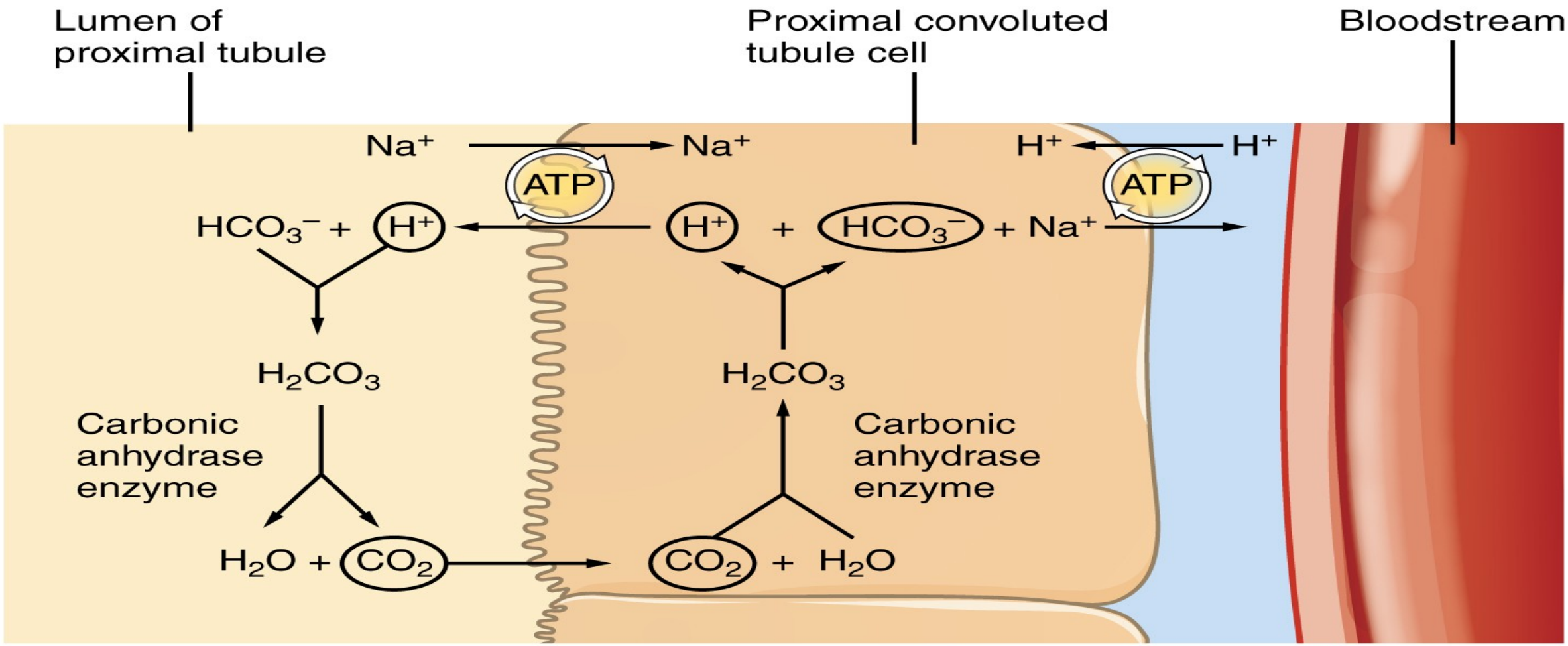
- Countertransport reabsorption of Na^+ across the luminal membrane is accompanied by H^+ secretion via Na^+ - H^+ counter-transport.

- H^+ secretion is accompanied by HCO_3^-reabsorption.Na is reabsorbed as NaHCO3 .

:a) First half of The Proximal Tubule



:a) First half of The Proximal Tubule



:b) Late half of The Proximal Tubule

- Na^+ is reabsorbed with chloride ion (Cl^-) as NaCI.

2- Loop of Henle

- ***Thin descending limb:***

- Reabsorb water, but has no capacity to reabsorb Na^+ as the Na^+ transport proteins or channels are absent from luminal membrane.
- The tubular fluid osmolarity increases as it descends.

: Loop of Henle -2

- ***Thin ascending limb:***

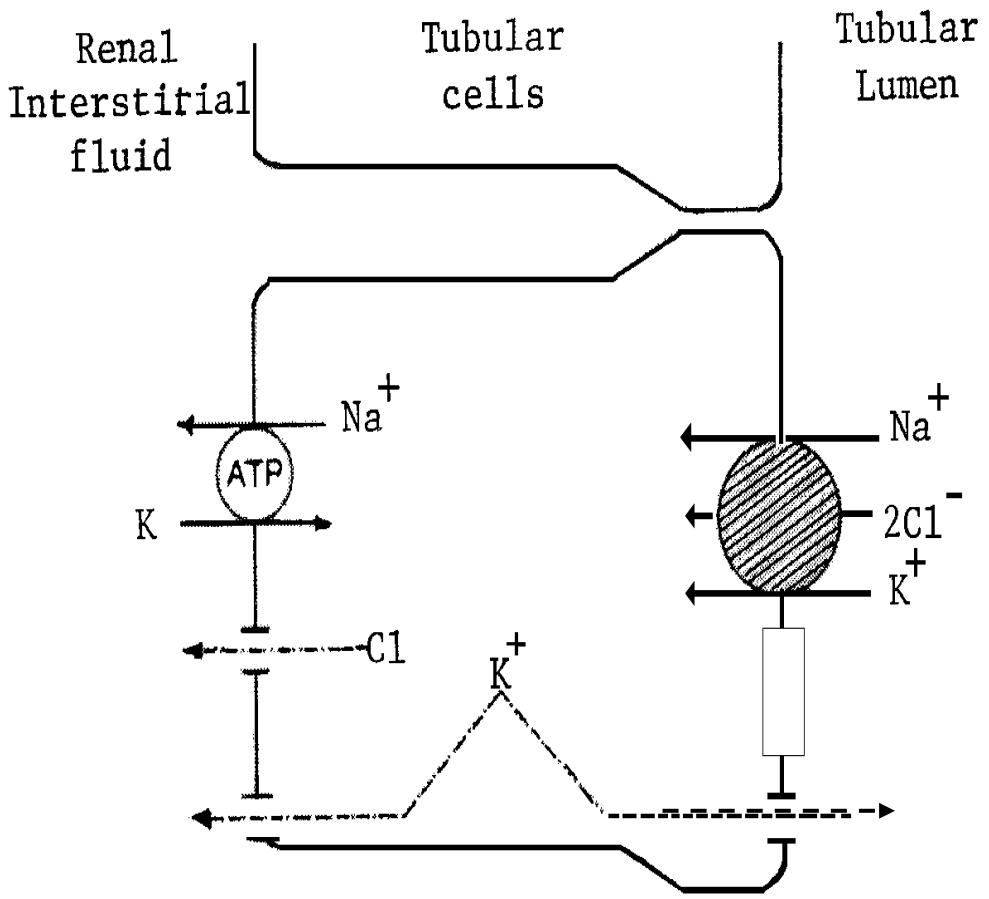
- NaCl diffuses passively from tubule to interstitum by concentration gradient.

- The thin ascending limb of the loop of Henle is impermeable to water. As a result, tubular fluid [Na+] and tubular osmolarity decrease .

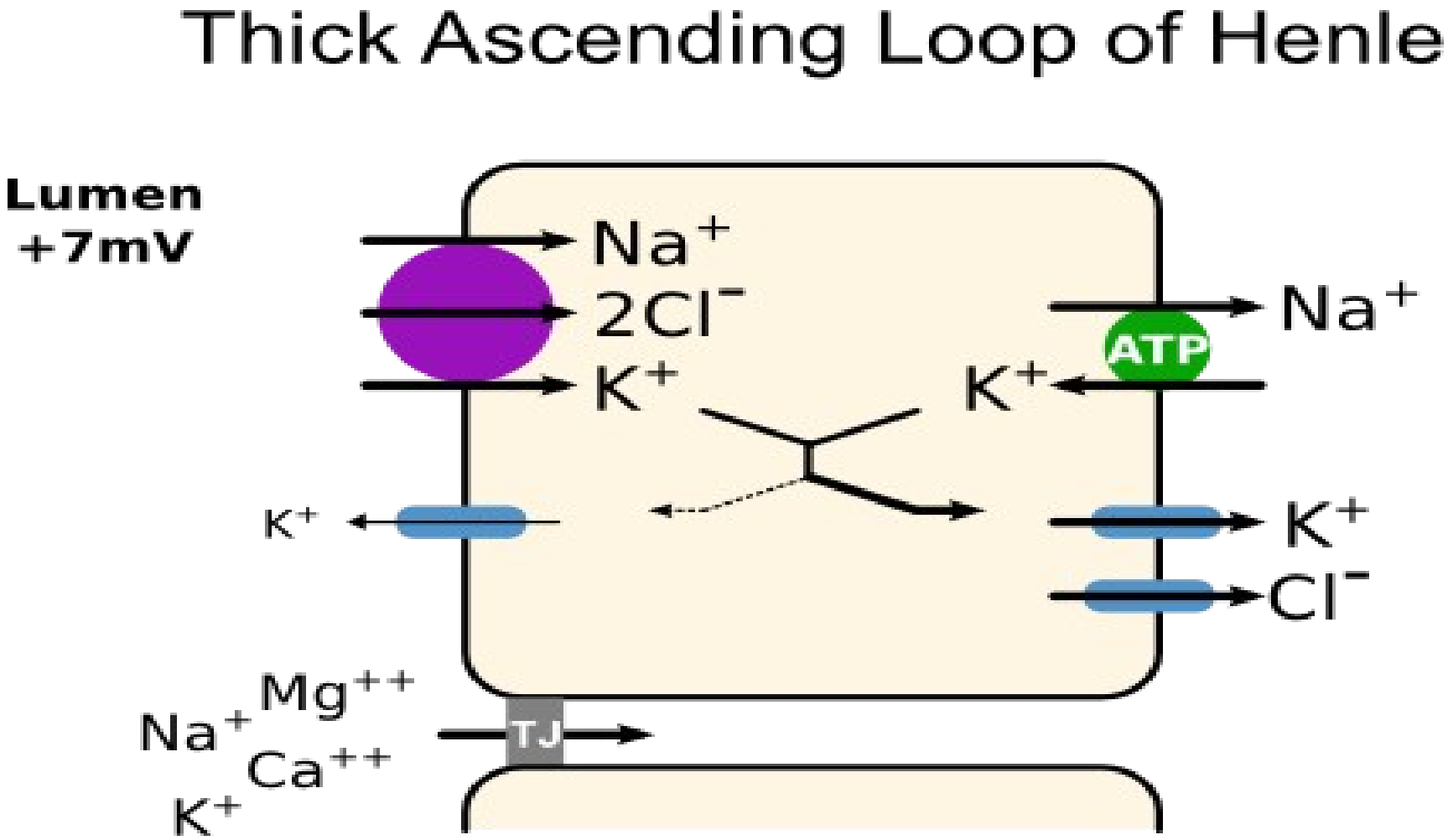
: Loop of Henle -2

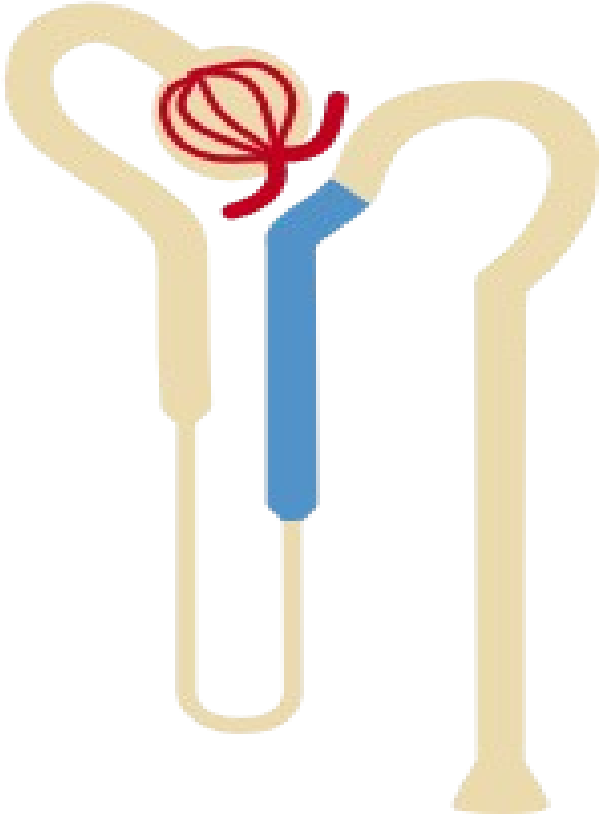
- **Thick ascending limb :**

- 25% of the filtered load of Na^+, K^+, and Cl^- are reabsorbed by co-transport mechanism, that co-transports one Na^+ one K^+ and two Cl^- from the lumen into the cells.



: Loop of Henle -2





: Loop of Henle -2

- **Most of the K^+ that enters the cell refluxes back into the lumen via K^+ channels and it serves two purposes:**

- It ensures a sufficient concentration of K^+ for optimal function of the co-transporter.

- The resulting net positive potential in the lumen facilitates paracellular reabsorption of several cations including Na^+, K^+, Ca^{++}, and Mg .

:Bartter's Syndrome

- **Cause**:
- Defect in the Na^+ - K^+ - 2 Cl^- cotransporter in the luminal membrane of the thick ascending limb □□Loss of Na^+, K^+, Cl^-, and ***calcium.***

- **Manifestations**:
- - Renal salt wasting Na^+ , K^+ ,CL^-

- Volume depletion
- Hypercalciuria
- Hypokalemia
- Metabolic alkalosis

Early distal tubule -3

- Reabsorption NaCl by a Na^+-Cl^- cotransporter.

- Is impermeable to water, as is the thick ascending limb. Thus, reabsorption of NaCl occurs without water which further dilutes the tubular fluid.

:Late Distal Tubule and Collecting Duct -4

- The principal cells are responsible for reabsorption of Na^+ in exchange with K^+ secretion.

- Rreabsorption of Na^+ is controlled by aldosterone.

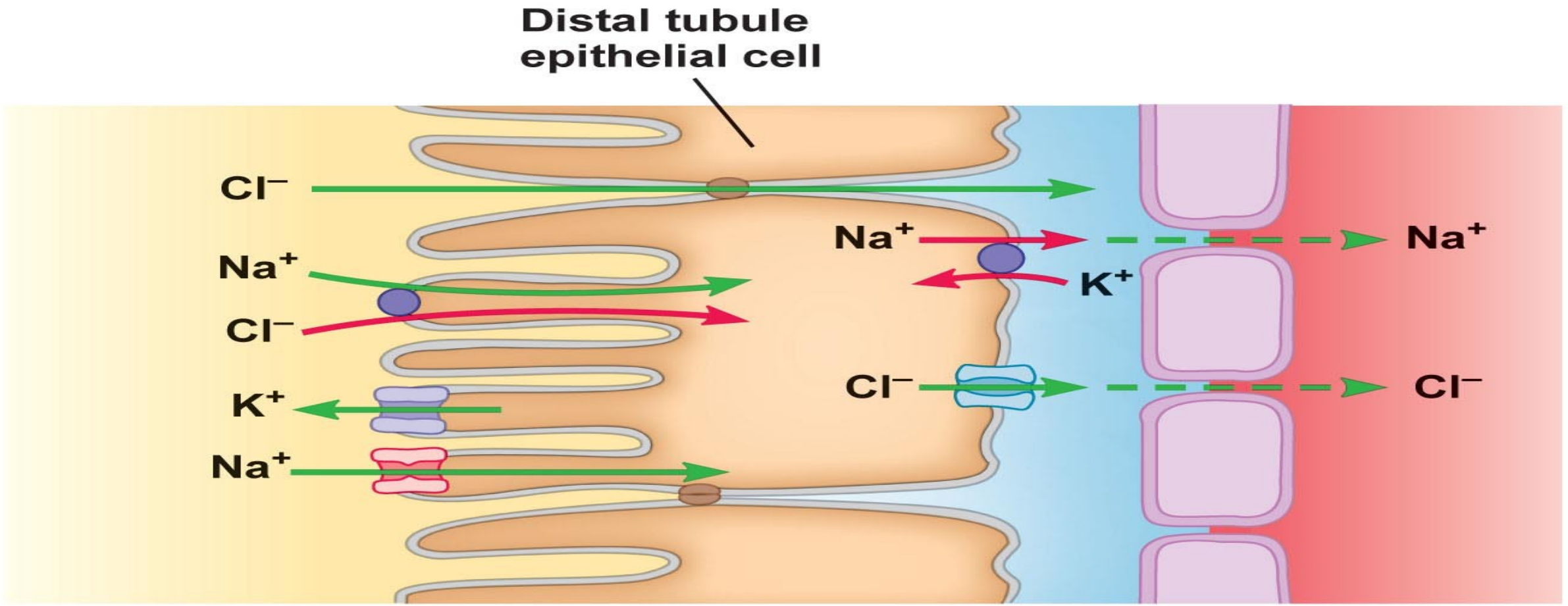
:Late Distal Tubule and Collecting Duct -4

Mechanism:

- Na^+ diffuses into the principal cells through Na^+ channels in the apical membrane, while K^+ diffuse into the tubular fluid across luminal membrane down its concentration gradient.

- . The anion that accompanies Na^+ is mainly Cl^- through paracellular route.

:Late Distal Tubule and Collecting Duct -4



(b) Sodium reabsorption in the distal tubule

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Glomerulotubular Balance

- **Definition:**
- An increase in GFR causes an increase in the reabsorption of sodium and consequently of water.

- **Site**:

- The main site is the proximal convoluted tubule. Loop of Henle also shares.

- The mechanism occurs independent of hormones and can occur in isolated kidney.

- - The proximall tubules reabsorb a constant percentage of the filtered Na^+ and water (2/3 or 65%) rather than a constant amount.

Glomerulotubular Balance

Importance:

a- It helps to prevent overloading of the distal tubular segment when GFR increase.

b- lt prevents inappropriate losses of Na^+ and water in the urine that can occur as a result of sudden increase in GFR.

- Thus, increased GFR increases the amount of Na^+ filtered and this increases the amount reabsorbed leading to a slight increase in Na^+ excretion .

Glucose Reabsorption

Site :

- Early portion of the proximal convoluted tubule.

Mechanism

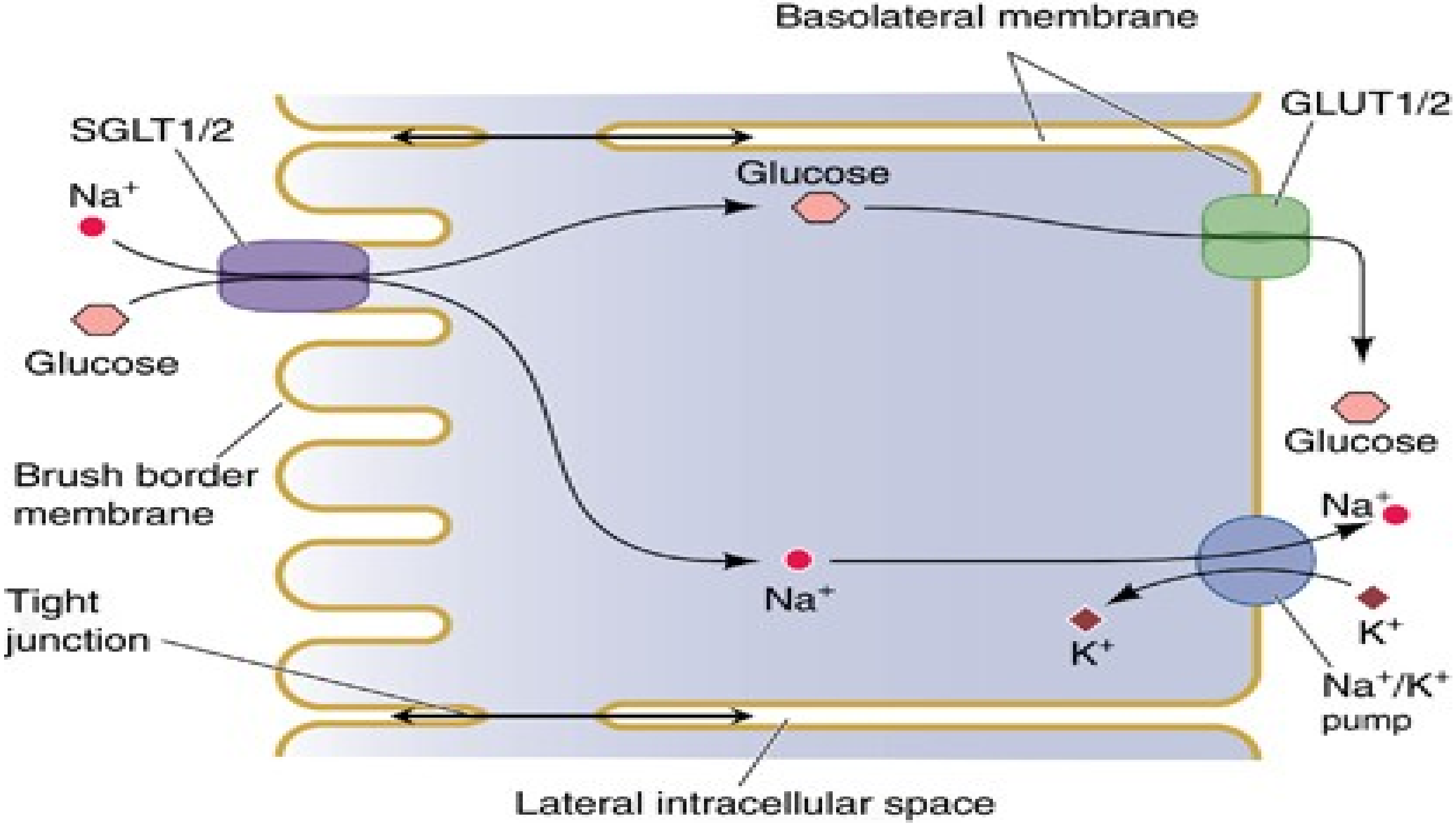
- Secondary active transport, i.e. secondary to the primary active transport of Na^+:

- At the luminal border:

Glucose and Na^+ bind to a common carrier SGLT-2 (Sodium-dependent glucose transporter) in the luminal membrane. As Na^+ moves down its chemical and electrical gradient, glucose is carried into the cells.

- At the basolateral border:

Glucose is carried into the interstitium by facilitated diffusion down chemical gradient. The carrier is GLUT-2 (glucose transporter)


Basolateral membrane
SGLT1/2
GLUT1/2
Na+
Glucose
Glucose
Glucose
Brush border membrane
Na+
Na+
Tight junction
K+
K+
Na+/K+ pump
Lateral intracellular space

Tubular Transport Maximum(T_m) of Glucose

T_{mG} : The maximum amount of glucose (in mg) that can be reabsorbed by the renal tubules per minute.

- TmG is determined by the number of glucose transporters in the proximal tubule.

- Value: T_{mG} : 300 mg / min in female.

  375 mg / min in male.

Renal Threshold of Glucose

The plasma level at which glucose first appears in the urine than the normal minute amounts.

- **Value:**

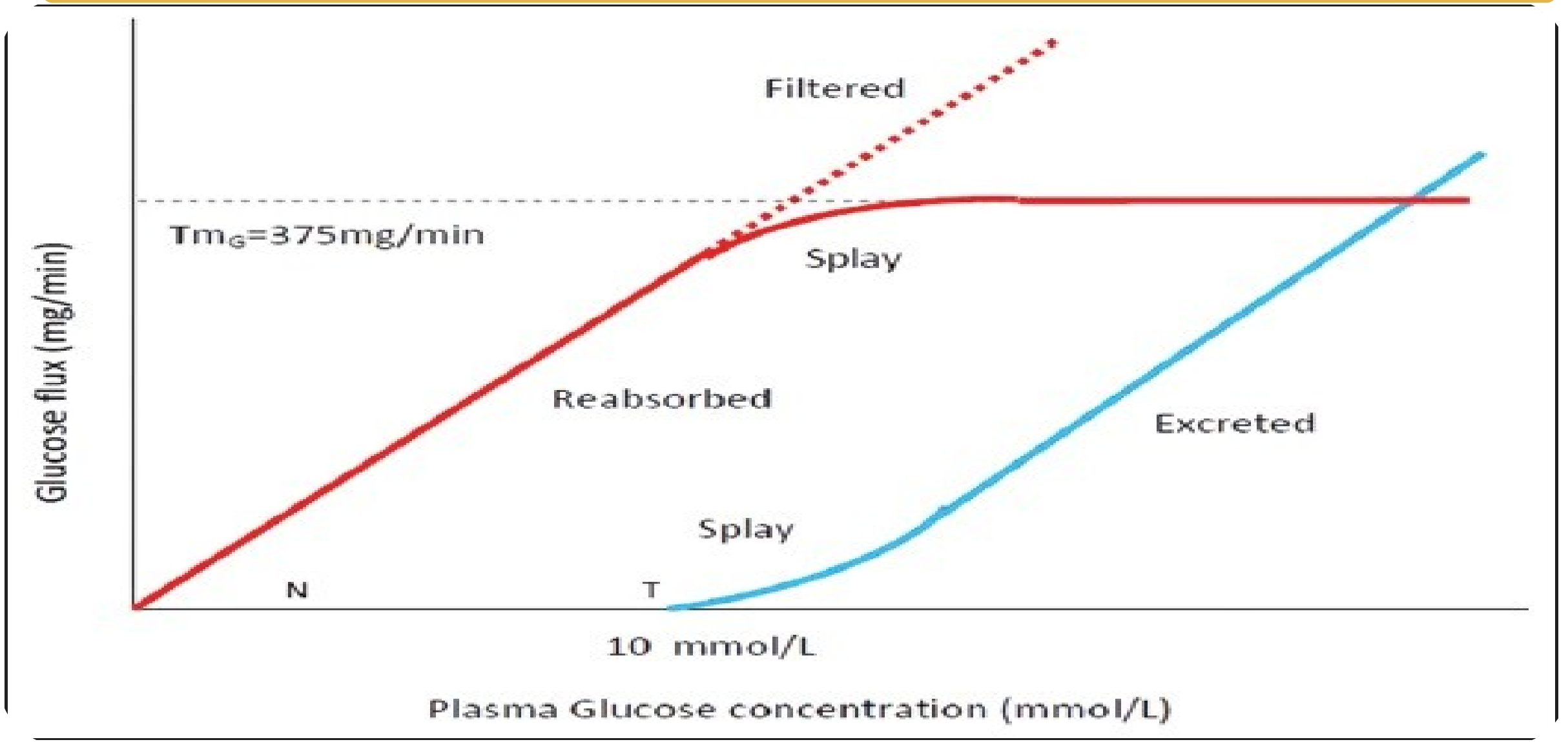
  - Arterial blood: 200 mg / dl
  - Venous blood: 180 mg / dl

Glucose Titration Curve and T_m

- Glucose titration curve depicts the relationship between plasma glucose concentration and glucose reabsorption.

- The filtered load of glucose and the excretion rate of glucose are plotted on the glucose titration curve .

Glucose Titration Curve and T_m:



Glucose Titration Curve and T_{mG}:

The titration curve is best understood by examining each relationship separately and then considering all three relationships together.

Filtered load of glucose:

- Glucose is freely filtered across glomerular capillaries l
- -Filtered load = GFR x [P] glucose.
- As the plasma glucose concentration is increased, the filtered load increases linearly.

Reabsorption of glucose:

- At the plasma glucose concentration less than 200 mg/dl, all of the filtered glucose is reabsorbed because Na^+ glucose transporters are plentiful. , i.e. reabsorption equals filtration.

- At the plasma glucose concentration above 200 mg/dl the reabsorption curve bends because some of the filtered glucose is not reabsorbed .

Reabsorption of glucose:

- At the plasma glucose concentrations above 300 mg/dl, the carriers are completely saturated and reabsorption reaches its maximal value T_m.

- Therefore, increases in plasma concentration above 300 mg/dL do not result in increased rates of reabsorption .

Titration Curve of Glucose

- To understand the curve for excretion, compare those for filtration and reabsorption as follows:

- Below plasma glucose concentration of 200 mg/dl, all of the filtered glucose is reabsorbed and none is excreted.

- Above plasma glucose concentrations of 200 mg/dl, the carriers are nearing the saturation point. Most of the filtered glucose is reabsorbed, but some is not; the glucose that is not reabsorbed is excreted.

Titration Curve of Glucose

- Above 300 mg/dl, Tm is reached and the carriers are fully saturated.
- Therefore, as the plasma concentration increases the addition of filtered glucose cannot be reabsorbed and is excreted in the urine.
- The curve for excretion now increases linearly paralleling that for filtration.
- The plasma glucose concentration at which glucose is first excreted in the urine is called threshold, .

Titration Curve of Glucose

- The T_m for glucose is approached gradually, rather than sharply producing the splay. . Splay is the region of the reabsorption curve between threshold and T_m and occurs between plasma glucose concentration of approximately 200 and 300 mg :dL

Titration Curve of Glucose

- ***Splay*** is due to heterogeneity of the nephrons: Tm reflects the average T_m of all nephrons, yet all nephrons do not have exactly the same T_m. Some nephrons will reach Tm at lower plasma concentration than others, and glucose will be excreted in the urine before the average Tm is reached.

Glycosuria

It is excretion of glucose in urine.

Causes:

1) Diabetes Mellitus:

Glycosuria occurs when the blood glucose level exceeds renal threshold.

2) Renal glycosuria:

Glycosuria occurs at normal plasma glucose level. The renal threshold for glucose is lowered below 180 mg % due to congenital defect in the glucose transport mechanism in the renal. Tm is markedly decreased

Lecture Quiz

Question 1 Which of the following is the primary site of Na^+ reabsorption in the kidney ?

a) Glomerulus.
b)Proximal convoluted tubule.
c)Thick ascending limb of loop of Henle.
d) Collecting duct.
e)Juxtaglomerular apparatus.

Lecture Quiz

Question 2 Which of the following describes glucose reabsorption by the kidney ?

a) Occurs by facilitated diffusion at luminal border.
b) Active transport of glucose across the basolateral border occurs by Na^+-K^+ ase.
c) Characterized by transport maximum (Tmg) of 220 mg /100 mLplasma
d) The filtered load and reabsorption rate are the same at plasma glucose concentration below the renal threshold.
e) Occurs at all segments of the renal tubule.

SUGGESTED TEXTBOOKS

1. Ganong’s Review of Medical Physiology 25 th Edition from page 679 to 682.
2. TEXTBOOK OF Medical Physiology 11 th Edition GUYTON& HALL from page 330 to 336.